RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOOST VAN NEERVEN

Appeal 2007-1070
Application 09/467,901
Technology Center 1600

Oral Hearing Held: April 24, 2007

Before DONALD E. ADAMS, DEMETRA J. MILLS, and
RICHARD M. LEBOVITZ, Administrative Patent Judges

On Behalf of the Appellant:

MARYANN T. PUGLIELLI, ESQ.
Finnegan, Henderson, et al.
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The above-entitled matter came on for hearing on Tuesday, April 24, 2007, commencing at 2:30 p.m., at The U.S. Patent and Trademark Office, 600 Dulany Street, 9th Floor, Alexandria, Virginia, before Jan M. Jablonsky, Notary Public.

CLERK: Calendar Number 24, Appeal number 20071070. Maryann Puglielli.

JUDGE ADAMS: Thank you. Good afternoon.

MS. PUGLIELLI: Good afternoon. How are you?

JUDGE ADAMS: Very good. How are you?

MS. PUGLIELLI: Good.

JUDGE ADAMS: Would you like to introduce your associate?

MS. PUGLIELLI: Excuse me?

JUDGE ADAMS: Introduce your associate?

MS. PUGLIELLI: Yes.

JUDGE ADAMS: And we're familiar with your issues and once you introduce your associate, you have 20 minutes.

MS. PUGLIELLI: Okay, great. Thank you. This is Andy Holtman.

JUDGE ADAMS: Greetings.

MS. PUGLIELLI: And what I would like to do -- so what I would like to do, if it please the Court, your Honors, is begin with an explanation of the most important parts of the invention. And because of those most important parts, I'd also like to provide you with a very short explanation of what the functions of IgE are as an antibody. And then conclude by going through the references and explaining how it is that we believe that the references are quite different from the invention.

So may I proceed with that, or --

JUDGE ADAMS: Quickly. I think we're pretty familiar with the function of IgE and the context of the claimed invention. So if you want to quickly go through that, that would be great.

MS. PUGLIELLI: Okay.

The invention unlike other more standard assays is seeking to provide very important information about exactly what is going on with the allergic immune response. And let me just interject that if, at any point, you want to ask questions about what I'm discussing, please feel free to stop me.

Other assays that don't employ receptors are not going to provide this information. Because in vivo, IgE exerts its function as part of the allergic response by bonding to the receptor on the cells and then the cells in turn activate.

The other thing that the invention seeks to do that the references are not approaching is trying to preserve the types of in vivo interactions that happen with IgE antibody and its receptors. And also trying to preserve those interfering interactions that can happen in vivo, so it may not necessarily be a clean interaction between the antibody and its receptor.

Now, with that said, of course, IgE exerts its function through two different receptors, a high-affinity receptor and a low-affinity receptor. And the high-affinity receptor is expressed on a certain group of cells and the low-affinity receptor is expressed in a certain group of cells. And depending on which cell that receptor is attached to, you will get a different reaction. So it's a very general, very quick example.

For the high-affinity receptor, which is really involved in rapid allergic responses, like anaphylaxis, for example, you can have histamine production, you can have IL10 production, you can have nerve growth factor production. And again the issue is not so much exactly what do these things do, but that you get a certain profile of -- of the cascade of events that is going to happen because of which receptor is involved.

In contrast, the low-affinity receptor, which deals more so with the long-term allergic response, can also do things like trigger histamine production, but it also can deal with cell migration. So inviting other cells to come to the site of the allergic response. It can also deal with antigen transport so that more antigen is transported, for example, through an intestinal wall and thereby enhancing the allergic response.

So when you think about the cellular events going on with the high-affinity receptor versus low-affinity receptor, they are very different things.

Now, going back to the invention, because the invention is using these receptors, and the claims invoke not only the potential usage of both receptors at the same time, but also the use of one receptor and then separately from the other receptor, it's going to provide the physician with an idea of what kind of allergic response is that patient prone to make.

JUDGE LEBOVITZ: But because the claim says and/or, it covers essentially three different embodiments, and all we have to find one embodiment obvious, because that's enough to make a claim unpatentable.

MS. PUGLIELLI: So with that said, again, a reference like, for example, Johansen, which is using an antibody in order to do the detecting of the IgE complex instead of using a receptor, is not going to be able to provide that kind of information.

JUDGE LEBOVITZ: Why not? What can't it provide? Because the Johansen reference was using anti-IgE directed against the FC. The claimed invention uses receptors. How -- FC1 or FC2. How is that interaction different? And what evidence do you have of the difference that

you get a different result when you use the FC1 or 2 to pull down an IgE versus using the anti-IgE to pull down an IgE complex?

MS. PUGLIELLI: Well, for example, in the Frank reference, and this was something that the examiner had brought out in the prosecution, in the Frank reference, the reference was discussing how an IgE receptor can have less cross-reactivity than using simply an antibody that's binding to an IgE molecule. How the receptor can have higher sensitivity. So those types of facts, in terms of comparing the receptor versus the antibody, showed that the two really are not equivalent reagents, simply because they both have the propensity to bind IgE.

JUDGE ADAMS: So by combining Johansen and Frank, Frank actually motivates one to use an FC receptor rather than an antibody bound to the support structure?

MS. PUGLIELLI: Well, if the -- if the artisan were to read Frank and take that supposed teaching --

JUDGE ADAMS: The teaching you just relied upon, right?

MS. PUGLIELLI: Right.

JUDGE ADAMS: Okay.

MS. PUGLIELLI: And take that teaching and look at Johansen, Johansen uses an anti -- as you're saying -- uses an anti-FC IgE antibody. And so if Frank is teaching away from using that type of antibody and then the artisan looks at Johansen, which does exactly what Frank is telling you not to do, then there wouldn't be that motivation to combine them and say, oh, well, I should put a receptor in.

Frank really provides a laundry list of different types of reagents that you could use in the assays and it doesn't highlight any one of

them as being particularly beneficial over any other. Not only does it discuss potentially hundreds of thousands of different combinations of assay reagents, it also talks about and lists as a laundry list, you could do it in this format, that format, this format, that format.

JUDGE ADAMS: Other than the IgE FC, what does Frank teach for that particular binder for that particular IgE to this molecule?

MS. PUGLIELLI: Well, the thrust of Frank is that it's -- it focuses on the discovery, really, of the canine version of the high-affinity receptor. And most of the examples in Frank deal with how did we clone it, how do you express it? And then the description section of the reference really goes into well, here are a bunch of different assay formats, different ways in which you could do it, and you could use this canine receptor in those assay formats. But again --

JUDGE ADAMS: So notwithstanding all the other reagents that he might use in his -- in his assay, he talks about using the Fcε, right?

MS. PUGLIELLI: He talks about using the --

JUDGE ADAMS: Does he talk about any other molecule other than Fcε?

MS. PUGLIELLI: I'm sorry, could you say that again?

JUDGE ADAMS: Does he -- does he talk about any other molecule other than the Fcε receptor?

MS. PUGLIELLI: There are some embodiments in which he is just using the receptor alone to detect the presence of an antibody. There are some embodiments where he's trying to invoke the presence of a ligand as well.

Even in the situations where you think of all three of those components, again the way in which Frank discusses --

JUDGE ADAMS: Let's be clear. All three of which components?

MS. PUGLIELLI: A ligand, an IgE antibody and the canine receptor.

JUDGE LEBOVITZ: Can we just clarify, we're talking about Frank?

MS. PUGLIELLI: Yes, Frank.

JUDGE LEBOVITZ: And Frank is talking about the Fcε receptor?

MS. PUGLIELLI: Canine, yes. Yes.

JUDGE LEBOVITZ: But the claims which the examiner pointed out were not limited to human or any species or even mammalian. They just say, Fcε --

MS. PUGLIELLI: -- receptor.

JUDGE LEBOVITZ: Right.

MS. PUGLIELLI: To go back to your question about also why is it important to use the receptor as opposed to an antibody, for example, Figure 2 is justification. Which, if you don't have that before you, I can give you copies.

JUDGE ADAMS: No, we have it.

MS. PUGLIELLI: All three of you have it?

JUDGE ADAMS: The spec? Figure 2 of the specification?

JUDGE LEBOVITZ: Yeah, we have it.

MS. PUGLIELLI: So that provides actually a beautiful example of how an antibody detection, or an antibody mediated detection is going to differ from what a receptor can do.

JUDGE LEBOVITZ: Can you refer again to where you're talking about?

MS. PUGLIELLI: Figure 2.

JUDGE LEBOVITZ: Figure 2. Thanks. Sorry.

MS. PUGLIELLI: Figure 2. So looking at Figure 2, and I'll try to do this as quickly as possible, because your time is very precious.

In Figure 2, Figure 2 is using the assay of the invention. It's using B-cells that are expressing the CD23 receptor. And just to very quickly take you through each of these columns, that is if you're holding the -- if you're holding the table on its side so you can actually read what the axes say, the very top column is really a negative control, where you're taking serum from an allergic patient and you're not adding any allergen whatsoever. And so you expect that there is not going to be an interaction, because the interaction between IgE and the receptor is going to have to involve the ligand as well.

Now, the -- the next one is really a positive control, taking the allergic serum and then exposing to it the ligand that it's going to bind to, and then you've got the receptors. And of course, you see plenty of fluorescence coming out.

Then in the next sample, you're taking the allergic patient's serum and you're adding to it serum from a person who has undergone SAB treatment, which is a process of desensitizing a patient to an allergen that

they're allergic to. And you add the allergen. And you see that significantly the amount of fluorescence goes down there.

And then as another control, they have at the end SAB treated serum along with allergen.

Now, if you look at Figure 2.B, they are the same samples as I've just described them, except Figure 2.B is using an assay in which you are using an antibody to detect the complex. And what's of most importance is if you go to the third column or the third line, if you will, of Figure 2.B, you see that in that sample with the allergic patient serum, with the SAB treated serum and the allergen, there's still plenty of IgE there, that this antibody is detecting.

However, when it comes down to actually determining how much of that IgE is going to be participating in an immune reaction or an immune response, it's quite a different picture, that only the invention is going to show the physician, because the invention is using a receptor to detect the presence of these complexes, as normally would be in vivo, as opposed to using an antibody.

JUDGE ADAMS: Isn't that exactly what Frank says is the problem with using antibodies in this type of assay?

MS. PUGLIELLI: But again, Frank is only providing a very large laundry list --

JUDGE ADAMS: We had that discussion about reagents. And you were unable to tell me what, other than Fcε Franks taught to bind its antibody. All right, so there might be a whole laundry list of other agents that are possibly involved in these reagents. But what is it, I'll ask you one

last time, what is it other than Fcε receptor is Franks using to bind its antibody?

MS. PUGLIELLI: Well, the type of teaching of higher sensitivity and higher specificity is going towards the direction of trying to detect as much IgE as you possibly can, as opposed to being concerned with mimicking these interactions.

JUDGE ADAMS: Like nonspecific -- doesn't he talk about nonspecific binding?

JUDGE LEBOVITZ: Can I -- there are two kinds of assays that are being done. One is an assay that detects total IgE and another assay that detects a subclass of IgE which is specific for a particular antigen. And that depends upon whether you pull down all the IgE or whether you're only pulling down IgE that binds an antigen.

MS. PUGLIELLI: And even then --

JUDGE LEBOVITZ: But -- but both those embodiments are taught in Johansen. And what Frank is telling you, if you use an Fcε receptor antibody, you get even better results because you don't get cross-reactivity with IgG or any other nonspecific components.

That's sort of the prima facie case that the examiner is making. And I don't see how your results show that that prima facie case has a hole in it.

MS. PUGLIELLI: Well, the question would be, if one were to take a receptor and put it into the method of Johansen, what would trigger the artisan to make only that substitution and not to substitute any of the other components that are in Frank, too, without having to employ hindsight,

looking at the invention and saying, in retrospect, that it would be obvious. And, of course, that would be an inappropriate conclusion to make.

JUDGE ADAMS: Okay, well, Franks makes a comparison between anti-FC Ig and using the Fcε receptor, correct?

MS. PUGLIELLI: Yes, again, for the purposes of trying to optimize --

JUDGE ADAMS: What other reagent is there disclosed in Franks where he distinguishes between some advantage between it and something else?

MS. PUGLIELLI: Between?

JUDGE ADAMS: You're saying there's no motivation to selectively take Frank's teaching of the advantage of using Fcε receptor over the use of an anti-FC antibody. You're saying that -- that teaching that teaches that advantage, why would one just pick that one and not any other reagent and make that substitution from Franks into Johansen?

MS. PUGLIELLI: That --

JUDGE ADAMS: My question to you is, what other reagents, other than the Fcε receptor, does Franks teach as having an advantage over something that Johansen used?

MS. PUGLIELLI: Well, the -- I mean, the -- Frank focuses mostly on the receptor. But in terms of looking at the invention as a whole, it's not only an issue of using the receptor; it's also an issue of preserving these interactions that happen in vivo between the antibody and the receptor. In addition to preserving interfering interactions that happen. For example, CD21 also has the ability to bind to the low affinity receptor. If CD21 were

present in the sample, CD21 could compete for binding with the IgE to that receptor.

Interference interactions like that, there is a teaching in Frank that says you certainly could treat the sample to remove those kind of interfering particle. So again, that would demonstrate that what Frank really is going after is, regardless of the discussion of a receptor, is that Frank is going after optimizing detection of IgE and not so much trying to preserve these interactions and these "contaminants" in the sample, if you will, that might interfere with that detection. The invention wants to preserve those things.

JUDGE LEBOVITZ: And how does preserving those interactions make it better? I mean, the way I was looking at it, it looked like the preservation of the interactions was only allowing you to capture a particular class of IgE, which was specific for an antigen.

MS. PUGLIELLI: Well, it goes beyond that.

JUDGE LEBOVITZ: Okay.

MS. PUGLIELLI: Because what you were talking about, for example, of using an antibody to just simply capture all IgE and then using an antibody to capture IgE that deals with a specific ligand, or ligand, the invention goes a significant step further in that you're not just asking which of those IgEs bind to a particular Ligand, which of them are present in a sample. You're asking which of them can actually participate in an immune response and therefore which of them are going to be active.

For example, I would suggest that a physician who sees a very high level of IgE but knows, because of the results that the invention provides, that a significant percentage of that IgE is inactive is not going to

be as concerned with a patient showing that profile as he or she will be with a patient showing a moderate level of IgE. But a high proportion of that being active in an immune response.

JUDGE LEBOVITZ: I understand.

MS. PUGLIELLI: Now, the other issue as far as the prosecution is concerned is that the examiner really hasn't provided a basis for an expectation of success in making this combination. Most of what we have been talking about, I think, is dealing with the motivation to combine. And, of course, that is another required element of obviousness, that there be an expectation of success.

JUDGE ADAMS: So your argument is that the Fcε receptor, one wouldn't expect to be able to bind IgE with the Fcε receptor when it's bound to a solid support? Is that your argument?

MS. PUGLIELLI: For which reference in particular?

JUDGE ADAMS: The combination of Franks and Johansen. So if we can get past this idea that one would modify Johansen by putting an FC receptor on its -- on its solid base, even if we could get past that, your argument is there's no expectation of success that this FCE receptor would continue to bind IgE?

MS. PUGLIELLI: Well, the premise being that again, in vivo, you're not having a receptor sitting immobilized on a platform. These receptors are sitting on cells which, in turn, are in a dynamic state within the host. And again, the invention mimics this.

So it's not so much an issue of whether we believe it would work or it wouldn't work. If you use something immobilized to a surface,

that removes it from the realm of the invention because you're not mimicking these in vivo interactions.

JUDGE ADAMS: Any other arguments with regard to the first obviousness rejection?

MS. PUGLIELLI: The combination of Johansen, Frank and Johnson was the first --

JUDGE ADAMS: Correct.

MS. PUGLIELLI: I'll just try to recount what we've discussed to make sure -- well, the other thing that I would add is that Johnson is only discussing CD23 in -- you know, what the examiner refers to in Johnson is really just an overview of CD23, the fact that it can happen in soluble forms and that the fact that the soluble forms can, in turn, regulate levels of IgE. And that is something very different from employing CD23 in an assay to detect IgE.

And the rest of that reference really deals with trying to inhibit the cleavage of CD23 from the surface of a cell and how that would beneficially keep down the levels of IgE. So the type of teaching in Johnson, as far as the background of CD23, I mean, that was discovered in the late '80s, and that kind of background is really known and it doesn't contribute anything of relevance to the context of the invention, aside from just providing a general teaching that one could obtain anywhere, really.

JUDGE ADAMS: Did you want to make comments about the combination with Arnold?

MS. PUGLIELLI: Yeah, as far as Arnold is concerned, again, it's a similar situation as with Johnson, in the sense that the examiner is pointing to a very general background paragraph that just talks about assays

that employ a separation step. And for that matter, it talks about an assay in which you have an antibody that is again immobilized to a surface. It's not talking about receptors at all. It's not talking about detecting IgE at all. And again, there if you look at the entire thrust of the reference, you're talking about a reference that's identifying new types of labels that will change their stability when they are involved in a complex. Basically, you're trying to get rid of separation steps -- that's what Arnold is teaching -- and trying to go more into the realm of a homogenous assay system where you don't have to do these separation steps.

Again, that is far removed from the invention. It doesn't mention a receptor at all. And really has no nexus between the other two references, Johansen and Frank. And we've discussed Johansen and Frank together and, again, those fall apart because without hindsight, the skilled artisan would not know to only substitute an FC receptor. The skilled artisan would also potentially substitute many other of the types of reagents that Frank teaches, again, with both Johansen and Frank teaching towards maximizing identification of IGE in a sample, as opposed to doing an assay that's more reflective of what's going on in vivo.

JUDGE MILLS: The motivation for making the substitution of the receptor doesn't have to be the same and achieve the same result as the motivation of the appellant in this case, though. The case law is pretty clear on that. So --

MS. PUGLIELLI: Well, the fact would still remain, though, in order for you to come up with the invention from Frank 2, and Johansen, you would have to select a specific combination of all of the elements that are taught in Johansen and all of the elements that are taught in Frank 2.

And Frank may discuss using a canine FC1 receptor, but it lists all of the other ingredients in its assays. It basically lists many, many, many combinations of different assays that could be run, depending on which component that you linked to what kind of surface, what format is it, is it a radio-immunoassay, is it an Elisa? And it doesn't teach these different components and these different combinations and these different assay formats in a way that points the artisan towards this specific combination.

And again, if Frank were to say that using antibodies to do the detection is not the way to go, then without hindsight, what would point the artisan towards Johansen at all in terms of an assay format?

But in the absence of hindsight, there's nothing in Frank that is going to point the artisan to using this specific combination. There would be hundreds of thousands of different combinations based on the teaching of Frank in terms of developing different assay formats with different combinations of reagents in order to arrive at something close to the invention.

And there's just no -- there's nothing to point the way. They are taught equally in the reference.

JUDGE ADAMS: Any other questions?

JUDGE MILLS: No, I don't think so.

JUDGE ADAMS: Any other questions?

JUDGE LEBOVITZ: No.

JUDGE ADAMS: Okay, thank you.

MS. PUGLIELLI: Thank you very much.

(The hearing was concluded at 2:37 p.m.)